

In this Issue Extra – Light of my life

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Photobiology has been part of the *JID* from its inception. In April 1939 (*JID* 2:4351,1939), Stephan Epstein described experiments performed in six individuals, including himself, and introduced and defined the concept of photoallergy. After intradermal injection of sulfanilamide, natural sunlight or artificial light sources were applied and all individuals had an acute reaction. After 10 d, without further irradiation, two of the volunteers had an “urticarial reaction” that lasted for 10–14 d. This delayed reaction was defined as “photoallergic”, and the precise mechanisms by which UV light induces allergy are still under study 63 y after Epstein’s article.

Through the decades many *JID* articles have elucidated the interactions of light and the skin. In this issue there are two studies of the human epidermis after ultraviolet (UV) B irradiation. UV has multiple effects on the skin. It directly isomerizes urocanic acid from the *trans* isomer to the *cis* isomer, which acts as an immunosuppressant. UV also induces several cytokines and prostaglandin E₂ alters antigen presentation, increases TH2 responses, increases IL-10, and depletes Langerhans cells.

Kölgen and coworkers (p. 812) studied the decrease in Langerhans cells. UVB-induced apoptosis is one potential mechanism for the decrease in Langerhans cells, possibly due to UV-induced reactive oxygen species triggering apoptosis; another possibility emphasized in these studies is Langerhans cell migration. The buttocks, a favorite site for photobiologic studies, as even today they are relatively sun-protected, were irradiated with six minimal erythema doses (MED), and only a few apoptotic Langerhans cells were detected. The skin phototypes of the subjects were not described, but the MED varied over a 5-fold range.

To investigate the alternative hypothesis that migration was the cause of decreased Langerhans cells, migration was tested after skin on the inner forearm was irradiated and suction blisters, which cleave at the DE junction in the lamina lucida, were induced. (Interestingly, the MED on the forearms were 4–5 times higher than on the buttocks, suggesting the need to control for dose in addition to MED, as will be discussed below.) Langerhans cells in the blister roof and in the blister fluid were quantitated by CD1a immunostaining. Langerhans cells were increased in the blister fluid after irradiation, but not in the unexposed control skin. The maximum increase in the Langerhans cells in the blister fluid was 18 h after irradiation and was significantly correlated with the largest decrease in Langerhans cells in the epidermal blister roof. The vast majority of the apoptosis after UV was in non-Langerhans cells, which makes sense as only a small percentage of the living epidermal cells are Langerhans cells. Importantly, the fluid cells’ Langerhans cells contained thymidine dimers, a measure of UV irradiation, and were considered of epidermal origin.

The authors’ conclusion were interpreted (by me) to mean that Langerhans cells run away, or are chased away or in a more generic sense cannot maintain their epidermal position after UV exposure. This raises interesting questions about the normal growth factors and mechanisms that keep Langerhans cells in their suprabasal location in epidermis. Routine morphology can mistakenly lead one to envision that the epidermis is a static organ. The mechanisms for maintaining a complex epithelium with immigrant cells such as the Langerhans cells no doubt is related to a delicate and continuous balance among growth factors, receptors on the immigrant cells and their surrounding keratinocyte host cells, bi-directional migration and death of the Langerhans cell. Do the Langerhans cells run away to get repaired and come back another

day to play their role as immune sentries? Or is their presence in blister fluid an artifact from the method of blister formation? The authors discuss these possibilities and favor an outward migration of Langerhans cells from the epidermis, as occurs in some murine models. Further studies with blocking wavelengths below 290 nm have begun and will be necessary to more closely simulate solar irradiation. These experiments were done with 6 MED; experiments with lower MED will be important to determine the general importance of Langerhans cell migration in the response to UV.

Julius Caesar noted “Gallia est omnis divisa in partes tres” [All Gaul is divided into three parts]. Following and expanding on that lead, Fitzpatrick divided skin into five phototypes based on its intrinsic pigmentation and its response to sunlight. It was a great intellectual feat to make that initial classification; in this issue (p. 825) Sheehan and coworkers report some of the biologic bases of different skin types. The initial classification of 1975 has proven useful and the phenotypic characteristics of these skin phototypes have since been expanded in terms of their constitutive skin color, MED, reactivity to UV radiation, history of tanning, melanin pigmentation, photodamage, and susceptibility to skin cancer. This classification has been useful for the clinician, clinical investigator, patient, and esthetics industry. It will be a tremendous advance to understand phototypes at the molecular and physiologic level.

In this study, type II patients (burns easily, tans with difficulty) and type IV patients (tans well, burns rarely) were studied with solar stimulated irradiation with 0.65 MED and 2 MED. DNA damage was determined by monoclonal antibodies to thymidine dimers. Nineteen days of 2 MED per day (to simulate a beach holiday exposure, for those who escape the English winter) led to a light tan in type II skin and a light-to-moderate tan in type IV skin. Previous studies from this laboratory have concluded that thickening of the stratum corneum has no role in sun protection. DNA damage was a major focus of these studies, as that damage is used as a surrogate for the ability of light to induce malignancies. The doses studied approached those in a real life situation, 0.65 MED. That is a net MED dose and might be from low UV exposure or UV exposures while using sunscreen.

DNA damage was dose related with a reciprocity between dose and time so that the overall physical dose was the key variable. Type IV skin had higher DNA damage, which the authors conclude to be related to the higher dose of irradiation used to obtain erythema. This finding shows the importance of reporting both erythema and dosage. The persistence of erythema in xeroderma pigmentosum is well recognized, and persistent erythema per se may be a clinical indicator of susceptibility to skin cancer. Those with type II skin had persistence of erythema longer than those with type IV skin. In this study the authors conclude that tanning per se does not have a significant role in photoprotection, as after a period of “sensible” (0.65 MED per d) tanning, all subjects were tested with 2 MED and had protective factors in the range of 23 against thymidine dimer production.

These studies show the importance of dosing and measuring a variety of parameters in the UV response. Using doses that are more representative of safe and sensible exposure to the sun have the potential of defining the mechanisms protecting the skin under normal habits and practices. As society has not yet adopted the avoidance of excessive UV exposure, investigators need to understand the mechanisms of the acute and chronic damage in detail to develop effective interventions. Studies such as the ones in this issue advance us toward that goal.